II. REMARKS

Formal Matters

Claims 1, 2, 4, and 7-18 are pending after entry of the amendments set forth herein.

Claims 1-11 and 18 were examined and were rejected. Claims 12-17 were withdrawn from consideration.

Claims 1, 2, 4, 7, 10, 11, and 18 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to claims 1, 2, 4, 7, 10, 11, and 18 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: page 9, lines 12-16; page 4, line 31 to page 5, line 2; and page 11, lines 5-11. Accordingly, no new matter is added by these amendments.

Please replace claims 1, 2, 4, 7, 10, 11, and 18 with the clean version provided above.

Claims 3, 5, and 6 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Sequence compliance

The Office Action stated that the instant application fails to comply with the requirements of 37 C.F.R.§1.821-1.825, because sequences disclosed in Figures 5 and 6 are not accompanied by a reference to the relevant sequence identifiers.

Applicants submit herewith a Substitute Sequence Listing, which provides sequence identifiers for the sequences shown in Figures 5 and 6.

Objections to the specification

The specification was objected to because of the following informalities.

1. The Office Action stated that the specification does not contain an abstract of the disclosure as required under 37 C.F.R.§1.72(b).

Applicants respectfully request entry of the Abstract, provided herewith on a separate sheet.

2. The Office Action stated that the application in which the benefit of an earlier application are desired must contain a specific reference to the prior application in the specification or in an application data sheet.

Applicants respectfully request entry of the amendment to the specification shown above, which includes a reference to the prior applications.

Claim objections

Claims 1-7, 10, 11, and 18 were objected to because these claims recite non-elected groups.

Claims 1, 10, 11, and 18 are amended to refer to an LGR7 protein. Claim 2 is amended to refer to SEQ ID NO:06 or SEQ ID NO:08. Claims 4 and 7 are amended to refer to SEQ ID NO:05 or SEQ ID NO:07. As shown in Figures 3 and 4, and as discussed in Example 5, both SEQ ID NO:05 and SEQ ID NO:07 are LGR7 polynucleotides, encoding LGR7 polypeptides having amino acid sequences set forth in SEQ ID NO:06 and 08, respectively.

Rejection under 35 U.S.C.§101

Claims 1-11 and 18 were rejected under 35 U.S.C.§101 as allegedly lacking utility.

The Office Action stated that the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Applicants respectfully traverse the rejection.

As the Office Action acknowledged, the specification asserts that the human LGR7 polypeptide is a novel mammalian G protein coupled receptor (GPCR), characterized by the presence of extracellular leucine rich repeat regions. The specification asserts that the LGR7 polypeptide functions as a GPCR. Specification, page 3, lines 26-29.

The specification states that nucleic acids encoding mammalian LGR7 polypeptides are useful for producing LGR7 polypeptides, which polypeptides are asserted to function as GPCR. Specification, page 9, lines 20-27. Thus, the specification provides a credible, specific and substantial utility for the claimed polynucleotides.

The specification further states that the LGR7 polypeptides are useful for identification of a ligand for the GPCR; for screening for agonists and antagonists; and for the generation of functional binding proteins for the neutralization of the action of an endogenous ligand. Specification, page 11, lines 1-4; page 20, lines 8-14; page 2, lines 13-14; and page 21, lines 12-15. The claimed polynucleotides are useful for producing LGR7 polypeptides, which polypeptides are useful for identification of a ligand, for screening for agonists and antagonists, and for the generation of functional binding proteins for the neutralization of the action of an endogenous ligand. Thus, the specification provides a number of additional credible, specific and substantial utilities for the claimed polynucleotides.

The fact that the instant claims are supported by a credible, specific and substantial utility is further demonstrated in Hsu et al. ((2002) *Science* 295:671-674; "Hsu (2002)", a copy of which is provided herewith as Exhibit 1), a publication co-authored by inventors Sheau Y. Hsu and A.J.W. Hsueh. Hsu (2002) states that LGR7 binds relaxin, and that relaxin activates adenylate cyclase through G_S proteins upon relaxin binding. Hsu (2002), page 672, column 1, last paragraph; and Figure 1. Hsu (2002) further states that 7BP, a soluble ectodomain of LGR7, antagonizes the action of relaxin. Hsu (2002), page 673, Figure 4; and column 2. Thus, Hsu (2002) demonstrates that LGR7 (1) functions as a GPCR; (2) is useful for identification of a ligand for LGR7; (3) is useful for screening for agonists and antagonists; and (4) is useful for the generation of functional binding proteins that neutralize the action of endogenous ligands.

Applicants submit that the rejection of claims 1-11 and 18 under 35 U.S.C. §101 has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§112, first paragraph

Claims 1-11 and 18 were rejected under 35 U.S.C.§112, first paragraph, as allegedly lacking enablement. Claims 5, 6, and 11 were rejected under 35 U.S.C.§112, first paragraph, as allegedly lacking written description.

Enablement

Utility/enablement

The Office Action stated that since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention.

As discussed above, the specification provides a number of specific and substantial asserted utilities. Accordingly, those skilled in the art would know how to use the claimed invention.

Claims 5, 6, and 11

Claims 5, 6, and 11 recite an isolated nucleic acid comprising at least 18 or 50 contiguous nucleotides of the sequence consisting of SEQ ID NO:7, and a composition comprising at least 50 weight% of a mammalian protein consisting of LGR7 or a fragment thereof. The Office Action stated that it would have required undue experimentation for the skilled artisan to make and use the claimed invention. Applicants respectfully traverse the rejection.

Claims 5 and 6 are canceled without prejudice to renewal, thereby rendering this rejection of claims 5 and 6 moot.

The specification discusses various polypeptide fragments of LGR7, and their uses. Specification, page 9, line 5 to page 11, line 17. For example, the specification states that the extracellular domain of LGR7 are useful, e.g., in the neutralization of the action of endogenous ligands. Specification, page 11, lines 1-4; and page 21, lines 12-15. The specification discusses the structure of LGR7, and states that LGR7 contains an ectodomain. Specification, page 25, lines 15-19. As discussed above, Hsu et al. demonstrated that a soluble extracellular domain of LGR7 functions as an antagonist to LGR7, neutralizing the action of the ligand relaxin. Thus, those skilled in the art, given the guidance in the specification, would know which fragments of LGR7 would be expected to function as discussed in the specification.

The Office Action stated that the specification does not teach any functional or structural characteristics of the variants or fragments of the nucleic acid of SEQ ID NO:7 or the polypeptide of SEQ ID NO:8. However, based on the alignments provided in Figure 6, those skilled in the art could readily determine, without undue experimentation, those amino acids of LGR7 that could altered without changing the function of LGR7. The fact that those skilled in the art could readily identify amino acid residues essential for function is demonstrated in Hsu et al. ((2000) *Molec. Endocrinol.* 14:1257-1271; "Hsu (2000)", a copy of which is provided herewith as Exhibit 2), a publication co-authored by inventors Sheau Y. Hsu, Peter van der Spek, and Aaron Hsueh. Hsu (2000) states that, based on an alignment of the LGR7 amino acid sequence with those of other hormone-binding GPCR, point mutations were made in LGR7 that affected its function as a GPCR. Hsu (2000), page 1261, column 2, second full paragraph, to page 1263, column 2, end of Results section. Thus, given the information provided in the instant specification, those skilled in the art could readily and without undue experimentation identify and mutate amino acid residues important for the function of an LGR7 polypeptide as a GPCR.

Claim 18

Claim 18 recites a method for screening a sample for the presence of a ligand for LGR7. The Office Action stated that the skilled artisan would have to resort to trial and error experimentation to determine which samples or ligands might yield one with the desired activity. Applicants respectfully traverse the rejection.

Those skilled in the art were well aware, as of the priority date of the instant application, of a variety of assays to detect the presence of a binding event between a receptor and a ligand. Indeed, as discussed above, Hsu (2002) provides evidence that the LGR7 polypeptide binds relaxin. Thus, those skilled in the art could, without undue experimentation, screen a sample for the presence of a ligand for an LGR7 polypeptide.

Written description

Claims 5 and 6 are canceled without prejudice to renewal, thereby rendering this rejection of claims 5 and 6 moot.

The Office Action stated that the description of one nucleic acid species (SEQ ID NO:7) and one LGR7 polypeptide species (SEQ ID NO:8) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all variants and fragments with at least 18 or 50 contiguous nucleotides of the sequence consisting of SEQ ID NO:7 or all fragments of protein consisting of the amino acid sequence of SEQ ID NO:8. Applicants respectfully traverse the rejection.

The specification provides the nucleotide and amino acid sequences of at least two LGR7 polypeptides. As shown in Figure 5, the polynucleotides identified as SEQ ID NO:05 and SEQ ID NO:07 encode the polypeptides identified as SEQ ID NO:06 and 08, respectively. Both SEQ ID NO:06 and 08 are LGR7 polypeptides. The specification states that the LGR7 polypeptides are encoded by splice variants. Specification, page 25, lines 15-25. Furthermore, as discussed above, the specification provides guidance for various fragments of LGR7 polypeptides, and their uses. Thus, the specification provides adequate written description for the claimed polynucleotides.

Conclusion as to the rejections under 35 U.S.C.§112, first paragraph

Applicants submit that the rejection of claims 1-11 and 18 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§112, second paragraph

Claims 1-11 and 18 were rejected under 35 U.S.C.§112, second paragraph, as allegedly indefinite.

Claims 1-11 and 18

The Office Action stated that the acronyms LGR7, LGF4, and LGF5 render the claims vague and indefinite.

Claims 1, 10, 11, and 18 are amended to spell out the term "LGR7."

Claims 4-7

The Office Action stated that the phrase "complementary sequence thereof" renders the claims

indefinite. The Office Action stated that it is unclear whether the term refers to the entire nucleic acid sequence complement or variants and fragments of the complement. Applicants respectfully traverse the rejection.

Claims 5 and 6 are canceled without prejudice to renewal, thereby rendering the rejection of these claims moot.

Claim 4 recites an isolated nucleic acid according to claim 1, wherein the nucleotide sequence of said nucleic acid has the sequence of SEQ ID NO:05 or the complementary sequence thereof, or SEQ ID NO:07 or the complementary sequence thereof. The plain meaning of the phrase "the complementary sequence thereof" is clear, and refers to a nucleic acid that is the complement of the recited sequence, i.e., the complement of the entire sequence.

Similarly, the plain meaning of the phrase "the complementary sequence thereof" in claim 7 is clear. Claim 7 recites an isolated nucleic acid that hybridizes under stringent hybridization conditions to a nucleic acid having the nucleotide sequence of SEQ NO:05 or the complementary sequence thereof, or SEQ ID NO:07 or the complementary sequence thereof. The plain meaning of the phrase "the complementary sequence thereof" is clear, and refers to a nucleic acid that hybridizes under stringent conditions to the complement of the recited sequence, i.e., the complement of the entire sequence.

Accordingly, claims 4 and 7 are clear, and need not be amended.

Claim 3

Claim 3 is canceled without prejudice to renewal, thereby rendering the rejection of this claim moot.

Claim 7

The Office Action stated that stringency is relative, and the art does not recognize a single set of conditions as stringent.

Without conceding as to the correctness of this rejection, claim 7 is amended to recite an isolated nucleic acid that hybridizes at 50°C or higher in a solution of 15 mM sodium chloride, 1.5 mM sodium citrate.

Claim 11

The Office Action stated that the term "50 weight%" is a relative term which renders the claim indefinite.

Without conceding as to the correctness of this rejection, claim 11 is amended to recite that the

LGR7 protein is at least about 80% pure.

Claim 18

The Office Action stated that the terms "binding event" and "mimetic" in claim 18 are indefinite.

Without conceding as to the correctness of this rejection, claim 18 is amended to recite "binding between said receptor and ligand," and to delete the phrase "a mimetic thereof."

Applicants submit that the rejection of claims 1-11 and 18 under 35 U.S.C. §112, second paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§102(b)

Claims 5 and 6 were rejected under 35 U.S.C.§102(b) as allegedly anticipated by Hillier et al. (Accession No. AA122079).

Claims 5 and 6 are canceled without prejudice to renewal, thereby rendering this rejection of claims 5 and 6 moot.

Applicants submit that the rejection of claims 5 and 6 under 35 U.S.C. §102(b) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STAN084.

Respectfully submitted,
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Date: Feb. 3, 2003

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Cancel claims 3, 5, and 6 without prejudice to renewal.

Please enter the amendments to claims 1, 2, 4, 7, 10, 11, and 18, as shown below.

1. (Amended) An isolated nucleic acid encoding a mammalian leucine-rich repeat-containing G-protein coupled receptor 7 (LGR7) protein [selected from the group consisting of LGR4, LGR5 or LGR7] , wherein the LGR7 protein comprises an amino acid sequence having at least 80% amino acid sequence identity to the sequence set forth in SEQ ID NO:08.

2. (Amended) An isolated nucleic acid according to Claim 1, wherein said mammalian protein has the amino acid sequence of [SEQ ID NO:2, SEQ ID NO:04,] SEQ ID NO:06 or SEQ ID NO:08.

4. (Amended) An isolated nucleic acid according to Claim 1, wherein the nucleotide sequence of said nucleic acid has the sequence [selected from the group consisting of: (a) SEQ ID NO:1 or the complementary sequence thereof; (b) SEQ ID NO:03 or the complementary sequence thereof; (c)] set forth in SEQ ID NO:05 or the complementary sequence thereof [; and (d)] or the sequence set forth in SEQ ID NO:07 or the complementary sequence thereof.

7. (Amended) An isolated nucleic acid that hybridizes under stringent conditions at 50°C or higher in a solution of 15 mM sodium chloride, 1.5 mM sodium citrate to a nucleic acid having the nucleotide sequence [selected from the group consisting of: (a) SEQ ID NO:1 or the complementary sequence thereof; (b) SEQ ID NO:03 or the complementary sequence thereof; (c)] set forth in SEQ ID NO:05 or the complementary sequence thereof [; and (d)] or the sequence set forth in SEQ ID NO:07 or the complementary sequence thereof.

10. (Amended) A method for producing a mammalian leucine-rich repeat-containing G-protein coupled receptor 7 (LGR7) protein, wherein the LGR7 protein comprises an amino acid sequence having at least 80% amino acid sequence identity to the sequence set forth in SEQ ID NO:08 [selected from the group consisting of LGR4, LGR5 and LGR7], said method comprising:

growing a cell according to Claim 9, whereby said mammalian protein is expressed; and

isolating said protein substantially free of other proteins.

11. (Amended) A purified polypeptide composition comprising [at least 50 weight % of the protein present as] a mammalian leucine-rich repeat-containing G-protein coupled receptor 7 (LGR7) protein [selected from the group consisting of LGR4, LGR5 and LGR7,] or a fragment thereof, wherein the LGR7 protein is at least about 80% pure, and wherein the LGR7 protein comprises an amino acid sequence having at least 80% amino acid sequence identity to the sequence set forth in SEQ ID NO:08.

18. (Amended) A method of screening a sample for the presence of a ligand for [a] leucine-rich repeat-containing G-protein coupled receptor 7 (LGR7) receptor [selected from the group consisting of LGR4, LGR5 and LGR7], said method comprising:

contacting said sample with [a] an LGR7 receptor, wherein the LGR7 receptor comprises an amino acid sequence having at least 80% amino acid sequence identity to the sequence set forth in SEQ ID NO:08 [selected from the group consisting of LGR4, LGR5 and LGR7or a mimetic thereof], and

detecting the presence of [a]binding [event] between said receptor and ligand in said sample.